UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,634	04/01/2004	Tania Kastelic	608352000100	8704

25226 7590 02/05/2008
MORRISON & FOERSTER LLP
755 PAGE MILL RD
PALO ALTO, CA 94304-1018

EXAMINER	
QIAN, CELINE X	
ART UNIT	PAPER NUMBER
1636	

MAIL DATE	DELIVERY MODE
02/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/814,634	KASTELIC ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,10,13-15 and 23-39* is/are pending in the application.

4a) Of the above claim(s) *10,13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,15 and 23-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9, 10, 13-15, 23-39 are pending in the application. Claims 10, 13 and 14 are withdrawn from consideration for being directed to non-elected subject matter. Claims 9, 15, 23-39 are currently under examination.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/07 has been entered.

Response to Amendment

The rejection of claims 9, 15, 23-29 under 35 U.S.C.112 2nd paragraph has been withdrawn in light of Applicant's amendment.

The rejection of claims 30-39 under 35 U.S.C.102 and 103 has been withdrawn in view of the new ground of rejection as discussed below.

The rejection of claims 9, 15, 23-29 under 35 U.S.C.112 1st paragraph is maintained for same reason as set forth in the office action mailed on 8/8/07 and further discussed below.

The rejection of claims 30-39 under 35 U.S.C.112 2nd paragraph is maintained for same reason as set forth in the office action mailed on 8/8/07 and further discussed below.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 15 and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In response to this rejection, Applicants argue that the limitation of "wherein said one or more 3'UTR sequence in said DNA expression vector and said one or more 3'UTR sequence in said control DNA expression vector are derived from the same gene" has support on page 27, lines 10-26 and page 28, lines 2-8 and Example 1. Applicants cite page 28, lines 5-8 to demonstrate the support of the limitation wherein the 3'UTR are from the same gene.

The above arguments are fully considered but deemed unpersuasive. The reasons for lack of description in the original specification for the claimed invention were discussed in detail in the office action mailed on 8/8/07. The examiner was mistaken in advisory action for stating the support on page 27 and 28 is sufficient for the claimed invention because the examiner overlooked the context of the cited portion. Upon further review, the cited portion was directed to DNA expression systems comprising a control and an expression testing system. However, the specification does not teach that DNA expression systems are present in the same cell line that is transfected by the two expression system, which is the claimed invention. As such, the newly added limitation lack support from the original specification. With regard to example 1, the issue is addressed in the previous office action. Briefly, the fact one working example in the

specification employs the THP-1 cell line co-transfected with two specific constructs PGL2_Neo and PGL2-β-galactosidase with 3'UTR sequence obtained from the same gene, that applicant may now wish to have for claim in any other cell lines and constructs broadly covered by the scope of the new claims after the filing date of the as-filed application, does not provide any legal basis showing that applicant is possesses the specific claimed subject matter as claimed in the new claims at the time the invention was made. In other words, new or amended claims which introduce elements or limitations such as a subgenus of the claimed cell line that comprises constructs, which have same 3'UTR between control and testing construct, and which are not supported by the as-filed disclosure as a whole, violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); In re Smith, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads). Therefore, for reasons discussed in the previous office action and above, this rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants have deleted the word "derived" in claim 9, but not in claim 30, therefore, it is rejected for same reason as stated in the previous office action.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9, 24-27, 29-34 and 36-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Zubiaga et al.

Zubiaga et al. disclose an expression vector comprising *c-fos* promoter operatively linked to globin gene, wherein several ARE isolated from *c-fos* is inserted into 3'UTR of the globin gene, pBBB+ARE, resulting in sets of cell lines comprises different expression constructs. Zubiaga et al. also disclose a control plasmid pBΔARE, in which it comprises the 53bp 3' UTR from c-fos inserted downstream of β-globin stop codon (see page 2220, 2nd col., Result section, 1st paragraph). Zubiaga et al. also disclose that a plasmid pRSV-lacZ, comprising a gene coding for expression of lacZ, 5'and 3'UTR for expression of said gene without mRNA instability sequence (see page 2221, 1st col., 2nd paragraph, lines 4-9), which serves as an internal control for correction for variations in transfection efficiency. Zubiaga et al. further disclose a second control plasmid pGB-ARE contains a fragment from GAPDH coding sequence inserted in frame within the 5' half of the globin coding region, and same elements from pBBB+ARE (see page 2221, bridging paragraph). Lastly, Zubiaga et al. disclose that the internal control construct, the second control plasmid pGB-ARE and the expression plasmid pBBB+ARE are co-transfected into NIH-3T3 cells (see page 2221, 1st col., 2nd paragraph, lines 1-4), and plasmid constructs

comprising different ARE sequence are transfected separately into NIH-3T3 cells (see for example, Figure 1). Therefore, Zubiaga et al. disclose the instantly clamed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zubiaga et al., in view of Banholzer et al.

The teaching of Zubiaga is discussed above.

Regarding claims 15 and 23, Zubiaga et al. do not teach an assay system for screening compounds which destabilize mRNA that comprises a cell line as claimed in claim 9 and a test compound, and wherein the cell line is stably transfected.

Banholzer et al. disclose that rapamycin promotes degradation of IL-3 transcripts at posttranscriptional level via 3' UTR (see page 3257, 2nd col., 1st paragraph). Banholzer et al. disclose two cell lines stably transfected with IL-3 expression system either with (VD1-M1) or without (VD1-M1ΔAU) mRNA instability sequence (3' UTR) (see page 3256, 1st col., lines 1-3). Banholzer et al. also disclose that following rapamycin and FK506 treatment, endogenous and exogenous wild type IL-3 decayed with very similar kinetics (see Figure 3b, left panel) whereas the exogenous mutant IL-3 mRNA level is not affected by either compound (Figure 3b, right panel, and 3c). The method and assay system disclosed by Banholzer et al. identifies rapamycin and FK506 as compounds that induce mRNA degradation.

It would have been obvious for one of ordinary skill in the art to develop an assay system as taught by Banholzer that is able to screen compounds such as rapalogs for their ability to modulating the mRNA instability sequence. Based on the teaching of Zubiaga, the ordinary skilled in the would have been motivated to screening compounds that would affect ARE sequence instability using the heterologous expression construct as disclosed in Zubiaga et al. One of ordinary skill in the art would also be motivated to use stably transfected cell lines because they are easy to maintain such that one does not have to do transfection every time to test a compound. The level of skill in the art is high. Absent evidence from the contrary, one of ordinary skilled in the art would have reasonable expectation of success to use the cell line taught by Zubiaga as a system to test compounds and make the cell line a stably transfected cell for said purpose. Therefore, the claimed invention would have been *prima facie* obvious at the time the invention was made.

Claims 28 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zubiaga et al., in view of Lemm and Ross (Molecular and Cellular Biology, 2002, Vol 22, No.12, pages 3959-3969).

The teaching of Zubiaga is discussed above. However, Zubiaga reference does not teach a coding region instability determinant as the instability sequence.

Lemm and Ross teach a 249 nucleotide coding region from c-myc destabilizes c-myc mRNA. Lemm and Ross also teach that said nucleotide sequence destabilizes beta-globin mRNA when inserted in frame within the coding region of said beta-globin gene (see page 3959, 2nd col., 2nd paragraph).

It would have been obvious to one of ordinary skill in the art to use the cell lines with constructs that have instability sequence as taught by Zubiaga et al. to test compounds that affect coding region instability determinants (CRD) from c-myc. One of ordinary skill in the art would have been motivated to do so for screening compounds that modulates the activity of the CRD. Absent evidence from the contrary, the ordinary artisan would have reasonable expectation of success to insert the CRD into a construct which can then be transfected into a cell line for testing compounds. Therefore, the invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joe Woitach Ph.D. can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER